

REMARKS

AMENDMENTS TO THE SPECIFICATION

Support for the amendments to the Specification may be found by reference to the Specification, as originally filed.

An amendment was made to the specification to include the Substitute Sequence Listing submitted herewith. Support for the Substitute Sequence Listing is described in the “Amendments to Sequence Listing” section within Applicants Remarks (see *infra*).

The paragraph beginning on page 1, line 35 and continuing onto page 2 was amended to append the appropriate SEQ ID NO assigned to the two sequences appearing within this paragraph, in this instance SEQ ID NO 42 and 43, as a consequence of adding these sequences to the Substitute Sequence Listing, to overcome the Examiners objection to the same. Corresponding amendments have been made to the originally submitted Sequence Listing as discussed *infra*. No new matter has been added.

The paragraph beginning on page 41, line 32 continuing onto page 42 was amended to append the SEQ ID NO assigned to the two sequences appearing within this paragraph, in this instance SEQ ID NO 44 and 45, as a consequence of adding these sequences to the Substitute Sequence Listing. Corresponding amendments have been made to the originally submitted Sequence Listing as discussed *infra*. No new matter has been added.

Example 1 was replaced with an amended Example 1 to delete the two referenced hyperlinks “ (<http://hmmer.wustl.edu/>)” and “ (<http://pfam.wustl.edu/>)” in order to address the Examiners objection to the same. No new matter has been added.

The paragraph beginning on page 1, line 23 was amended to correct a typographical error by replacing “recuritment” with “recruitment”. No new matter has been added.

The paragraph beginning on page 3, line 7 was amended to correct a typographical error by replacing “accummulate” with “accumulate”, in addition to deleting the double period at the end of this paragraph. No new matter has been added.

The paragraph beginning on page 3, line 21 was amended to correct a typographical error by replacing “asparigine” with “asparagine”. No new matter has been added.

The paragraph beginning on page 6, line 34 and continuing onto page 7 was amended to correct a typographical error by replacing “synthezised” with “synthesized”. No new matter has been added.

The paragraph beginning on page 9, line 31 was amended to correct a typographical error by deleting the double “of” on the first line of this paragraph. No new matter has been added.

The paragraph beginning on page 10, line 22 was amended to correct a typographical error by deleting the double “of” on the first line of this paragraph. No new matter has been added.

The paragraph beginning on page 11, line 5 was amended to correct a typographical error by deleting the double “of” on the third line of this paragraph. No new matter has been added.

The paragraph beginning on page 22, line 12 was amended to correct a typographical error by replacing “referred” with “referred”. No new matter has been added.

The paragraph beginning on page 26, line 32 continuing onto page 27, was amended to correct a typographical error by replacing “rescruitment” with “recruitment”. No new matter has been added.

The paragraph beginning on page 27, line 11 was amended to correct a typographical error by replacing “gastrointestinal” with “gastrointestinal”. No new matter has been added.

The paragraph beginning on page 28, line 10 was amended to correct a typographical error by replacing “diorders” with “disorders”. No new matter has been added.

The paragraph beginning on page 28, line 29 continuing onto page 29, was amended to correct a typographical error by replacing “gastrointesinal” with “gastrointestinal”. No new matter has been added.

The paragraph beginning on page 30, line 11 was amended to correct a typographical error by replacing “agonisits” with “agonists”. No new matter has been added.

The paragraph beginning on page 31, line 23 was amended to correct a typographical error by replacing “descussed” with “discussed”. No new matter has been added.

The paragraph beginning on page 32, line 22 was amended to correct a typographical error by replacing “homolgy” with “homology”. No new matter has been added.

The paragraph beginning on page 4, line 34 and continuing onto page 5 was amended to append the “Inhibitor of nuclear factor KappaB Alpha” definition for the “IkBa” abbreviation. Support for this amendment may be found in references known in the art prior to the filing date of Applicants instant specification. Specifically, Applicants refer the Examiner to the title and abstract of Rahman (Biochem. Plarm., 60(8)1041-1049 (2000); submitted concurrently herewith) for the definition of “NFkB” as “nuclear factor kappaB”. Applicants also refer the Examiner to Baeuerle et al (Science, 242:540-546 (1988); see entire article and title, and abstract, in particular; submitted concurrently herewith); to Brown et al (PNAS USA, 90:2532-2536 (1993); see entire article and

title, abstract, and background, in particular; submitted concurrently herewith); and Baldwin (Annu. Rev. Immunol., 14:649-81 (1996); see entire article; submitted concurrently herewith), for the definition of “IkB α ” as “inhibitor of NF κ B alpha”. Applicants note that “alpha” is the generally accepted scientific definition of the greek symbol “ α ” (see Websters Unabridged Dictionary, Second Edition, 1999, page 59; submitted concurrently herewith). Since Applicants have merely amended the specification to clarify information that is already known in the art, Applicants do not believe any new matter has been added.

AMENDMENTS TO THE SEQUENCE LISTING

Support for the amendments to the Sequence Listing may be found by reference to the Specification, as originally filed, and in the Sequence Listing, as originally submitted.

Specifically, the amendment to lines <140> and <141> of the Sequence Listing was made to make the Sequence Listing consonant with the assigned U.S. non-provisional serial number and filing date for the present application.

Support for the newly added sequence, SEQ ID NO:33, may be found in the specification as originally filed, and specifically, in Figures 2A-C. SEQ ID NO:33 represents the "Cyropyrin" protein sequence and is provided in Figures 2A-C. This sequence was previously assigned SEQ ID NO:33, although it was not present within the Sequence Listing as originally submitted. This sequence was added to ensure the Sequence Listing is consonant with the instant specification, as well as to ensure the Sequence Listing conforms to 37 C.F.R. 1.821-1.825.

Support for reassigning original SEQ ID NO:33 to 40 to SEQ ID NO:34 to 41 may be found in the Sequence Listing as originally submitted. The SEQ ID NOs of these sequences needed to be increased by one SEQ ID NO as a consequence of adding the Cyropyrin protein sequence into the Sequence Listing as SEQ ID NO:33. This amendment further ensures the Sequence Listing is consonant with the instant specification.

Support for the newly added sequences SEQ ID NO:42, 43, 44, and 45 may be found in the specification as originally filed, and specifically, in the paragraph beginning on page 1, line 35 and continuing onto page 2, and in the paragraph beginning on page 41, line 32 and continuing onto page 42. These sequences were added to the Sequence Listing, along with the appropriate lines <221> thru <223>, to conform to 37 C.F.R. 1.821-1.825, and to address the Examiner's objection to Applicants failure to include the same. Applicants note that the two "a's" in SEQ ID NO:42, the "o" in SEQ ID NO:43, and all of the amino acids in SEQ ID NO:44 and 45 were changed to "Xaa" in the Sequence Listing in order to conform to the Sequence Listing requirements and to afford Applicants with the ability to define each of these amino acids within the Sequence Listing.

Applicants make the statement that the contents of the Substitute paper and computer readable copies of the Sequence Listing submitted concurrently herewith are the same. Applicants also make the statement that no new matter is believed to be added. The Substitute paper and computer readable copies of the Sequence Listing are believed to comply with the requirements of 37 C.F.R 1.821 through 1.825.

STATUS OF THE CLAIMS:

Claims 24, 34, 35, and 37 were amended.

Claims 31, 32, 38, 39, 40, 41, 42, 43, and 44 were cancelled.

Claims 24 to 30, and 33 to 37 are pending.

Claim 24 was amended to change the “comprising” language to “consisting of” within Claim 24(e) in an effort to address the Examiners rejection to the same. Claim 24 was further amended to append the “and” term after Claim 24(d) in order to place Claim 24 in proper Markush form in consideration of the deletion of Claim 24(e). Applicants assert that this amendment was not made to overcome any issues related to the patentability of this claim and that Applicants right to equivalents of Claim 24 is reserved.

Claim 24 has been further amended to delete the phrase “including the start codon” within Claim 24(a), to delete the phrase “minus the start codon” phrase within Claim 24(b), and to delete the phrase “(antisense)” within Claim 24(e) to address the Examiners rejection to the same.

Claim 24 was further amended to change the spelling of the term “complimentary” in Claim 24(e) to its correct spelling as “complementary”.

Claim 34 was amended to change the “comprising” language to “consisting of” in an effort to address the Examiners rejection to the same. Applicants assert that this amendment was not made to overcome any issues related to the patentability of this claim and that Applicants right to equivalents of Claim 34 is reserved.

Claim 35 was amended to delete the “sequences” term to further clarify the subject matter encompassed by this claim. Applicants assert that this amendment was not made to overcome any issues related to the patentability of this claim and that Applicants right to equivalents of Claim 35 is reserved.

Claim 37 was amended to append the phrase “, wherein said heterologous nucleic acid sequence encodes the Fc domain of immunoglobulin” after the “heterologous nucleic acid” limitation. Support for this amendment is provided in original Claims 38 and 39. Applicants assert that this amendment was not made to overcome any issues related to the patentability of this claim and that Applicants right to equivalents of Claim 37 is reserved.

Claim 37 was further amended to delete the “further” term to place this claim into its proper context in consideration of the Claim 24 amendments discussed *supra*. Applicants assert that this

amendment was not made to overcome any issues related to the patentability of this claim and that Applicants right to equivalents of Claim 37 is reserved.

No new matter has been added.

I. Miscellaneous

a. Sequence Listing

In response to the “Notice to Comply With Requirements For Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures” submitted concurrently with the Examiners Office Action, Applicants amended the Sequence Listing and the relevant portions of Applicants specification. The resulting Substitute Sequence Listing in both hard copy and computer readable form, in addition to the appropriate statements are submitted concurrently herewith. Applicants believe the Examiners objections contained within this Notice have been overcome in consideration of these amendments, the submission of the Substitute Sequence Listing in both hard copy and computer readable form, in addition to the applicable statements submitted herewith.

b. Objections to the Specification

The Examiner has objected to Applicants specification because the disclosure “contains an embedded hyperlink and/or other form of browser-executable code. See for example page 200, the penultimate line.”

In response, Applicants have amended the specification to replace Example 1 in its entirety with an amended Example 1 that explicitly lacks the embedded hyperlink cited by the Examiner, in addition to another hyperlink contained within the same paragraph.

The Examiner has also requested that any minor errors, including typographical errors, be corrected. In response, Applicants have corrected any such errors that were found in the specification. Specifically, Applicants have corrected the typographical errors found within the paragraph beginning on page 1, line 23; paragraph beginning on page 3, line 7; the paragraph beginning on page 3, line 21; the paragraph beginning on page 6, line 34 and continuing onto page 7; the paragraph beginning on page 9, line 31; the paragraph beginning on page 10, line 22; the paragraph beginning on page 11, line 5; the paragraph beginning on page 22, line 12; the paragraph beginning on page 26, line 32 continuing onto page 27; the paragraph beginning on page 27, line 11; the paragraph beginning on page 28, line 10; the paragraph beginning on page 28, line 29 continuing onto page 29; the paragraph beginning on page 30, line 11; the paragraph beginning on page 31, line 23; and the paragraph beginning on page 32, line 22.

In consideration of these Amendments, Applicants believe the Examiners objections to the specification have been overcome.

c. Objections to the Claims

The Examiner has objected to Applicants Claims 40 to 44 alleging that these claims are in improper dependent form for failing to "further limit the subject matter of a previous claim". The Examiners objection to these claims has been rendered moot in consideration of Applicants cancellation of Claims 40 to 44.

d. Public Access to ATCC Deposit No. PTA-2766

Applicants representative hereby gives the following assurance by signature below:

Bristol-Myers Squibb Company, an assignee of the present application, has deposited biological material under the terms of the Budapest Treaty on the International Recognition of the Deposit of Micro-organisms for the Purposes of Patent Procedure with the following International Depository Authority: American Type Culture Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209. These deposits comprise the cDNA sequences encoding the HLRRSI1 polypeptide of the present invention. The deposit for the SILL1A clone of HLRRSI1 was made on November 15, 2000, and given ATCC Accession Number PTA-2679. The deposit for the SILL1B clone of HLRRSI1 was also made on November 15, 2000, and given ATCC Accession Number PTA-2674. In accordance with MPEP 2410.01 and 37 C.F.R. § 1.808, assurance is hereby given that all restrictions on the availability to the public of ATCC Accession Numbers PTA-2674 and PTA-2679 will be irrevocably removed upon the grant of a patent based on the captioned application, except as permitted under 37 C.F.R. § 1.808(b).

A copy of the ATCC Deposit receipts for Accession Numbers PTA-2674 and PTA-2679 is enclosed herewith.

II. Rejections under 35 U.S.C. § 112, first paragraph

a. The Examiner has rejected Claims 24, 29, 30, and 33 to 39 under 35 U.S.C. § 112, first paragraph. Specifically, the Examiner has rejected Claims 24, 29, 30, and 33 to 39 alleging that "The invention appears to employ a novel plasmid. Since the plasmid is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed plasmids' sequences are not fully disclosed, nor have all the sequences required for their construction been shown to be biblically known and freely available.

The enablement requirement of 35 U.S.C. § 112 may be satisfied by deposit of the plasmid or transformed. The specification does not disclose a repeatable process to obtain the vectors and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a deposit of the plasmid should have been made in accordance with 37 C.F.R. § 1.801-1.809.

Although the specification indicates that the deposits were made under the terms of the Budapest Treaty, the paragraph bridging pages 16 and 17, there is no indication of public availability of the deposits upon issuance of the patent. An affidavit or declaration by the applicant, or a statement by an attorney of record over his/her signature and registration number, stating that the specific microorganism(s) has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.”

In response, Applicants representative has provided the required assurance in the “Miscellaneous” section of Applicants Reply *supra*. Applicants believe the Examiners rejection of Claims 24, 29, 30, and 33 to 39 has been overcome in light of Applicants assurances provided herein.

b. The Examiner has rejected Claims 24 and 31 to 44 under 35 U.S.C. § 112, first paragraph, alleging that the disclosure is “enabling only for claims limited to the nucleic acid sequence encoding the protein of SEQ ID NO: 2 including SEQ ID NO: 1. The specification does not enable any person skilled in the art to make and use the invention commensurate in scope with these claims. The claims are broader than the enablement provided by the disclosure with regard to all possible nucleic acid sequences encoding 437 contiguous amino acid residues of SEQ ID NO: 2 which has any type of NFkB modulating activities, i. e., increasing or decreasing of any kind of NFkB (claims 24, 31, and 33-39). Also, claims 40-44 are drawn to any nucleic acid sequence encoding a protein having 80% sequence homology to SEQ ID NO: 2 having any type of NFkB modulating activities which includes natural and man-made insertion, deletion, substitution and combination thereof mutants. Factors to be considered in determining whether undue experimentation is required, are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.”

Applicants disagree. However, Applicants believe Applicants amendment of Claim 24 to change the “comprising” language to “consisting of” language; the deletion of Claim 24(e); the amendment of Claim 34 to change the “comprising” language to “consisting of” language; the amendment of Claim 37 to change the “further comprises a heterologous nucleic acid sequence” to “comprises a heterologous nucleic acid sequence encoding the Fc domain of immunoglobulin”; and the cancellation of Claims 31, 32, 38, 39, 40, 41, 42, 43, and 44 renders the Examiners rejection moot.

III. Rejections under 35 U.S.C. § 112 – Second Paragraph

a. The Examiner has rejected Claims 24, 25, 27, and 33 to 44 under 35 U.S.C. § 112, second paragraph, as being “indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” More particularly, the Examiner alleges that Claims 24, 40, and 44 “contains the undefined abbreviations and acronyms NFkB. Abbreviations and acronyms must be defined at least once in the claims.”

Applicants do not agree and point out that Applicants were unable to find any reference to such a requirement within the most recent version of the M.P.E.P. (Edition 8). However, the Examiners rejection of Claims 24, 40, and 44 has been rendered moot in consideration of the deletion of Claim 24(e) and the cancellation of Claims 40 to 44.

b. The Examiner has rejected Claim 24 under 35 U.S.C. § 112, second paragraph, as being “indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.” More particularly, the Examiner alleges “the phrases ‘amino acid 1 to 625 of SEQ ID NO: 2 including the start codon’, ‘amino acid 2 to 625 of SEQ ID NO: 2 minus the start codon’, and ‘(antisense)’ in claim 24; sections (a), (b), and (f), respectively, render the claims indefinite because the resulting claim does not clearly set forth the metes and bounds of the patent protection desired.”

Applicants disagree and point out that the phrases “including the start codon”, “minus the start codon”, and “(antisense)” were merely included to clarify the limitations already present within the claim and to assist the public in appreciating the metes and bounds of these claims. However, in the interest of facilitating prosecution, Applicants have amended Claim 24 to delete each of these phrases to address the examiners rejection of the same. Applicants believe the Examiners rejection of Claim 24, and in particular, the Examiners rejection of Claim 24(a), (b), and (f), has been

overcome in consideration of these amendments. Applicants also believe the Examiners rejection of Claims 25, 27, and 33 to 37 has also been overcome in consideration of these amendments since Claims 25, 27, and 33 to 37 depend from Claims 24(a), (b), and (f). The Examiners rejection of Claims 38 and 39 has been rendered moot in consideration of Applicants cancellation of Claims 38 and 39.

IV. Rejections under 35 U.S.C. § 102

a. The Examiner has rejected Claims 24, 25, 27, 29 to 38, 40 to 42, and 44 under 35 U.S.C. § 102(e) alleging that these claims are anticipated by Burford et al (International Publication No. WO 01/42288; filed December 7, 2000).

Applicants disagree. However, Applicants believe Applicants amendment of Claim 24 to change the “comprising” language to “consisting of” language; the deletion of Claim 24(e); the amendment of Claim 34 to change the “comprising” language to “consisting of” language; the amendment of Claim 37 to change the “further comprises a heterologous nucleic acid sequence” to “comprises a heterologous nucleic acid sequence encoding the Fc domain of immunoglobulin”; and the cancellation of Claims 31, 32, 38, 39, 40, 41, 42, 43, and 44 renders the Examiners rejection moot.

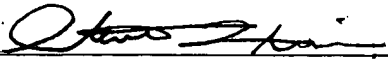
Applicants believe that all of the Examiners rejections and objections have been overcome and that all of the pending claims before the Examiner are in condition for allowance. An early Office Action to that effect is, therefore, earnestly solicited.

A three-month extension is hereby requested pursuant to 37 CFR §1.136(a). Please charge Deposit Account No. 19-3880 in the name of Bristol-Myers Squibb Company in the amount of \$950 for payment of the extension fee.

If any fee is due in connection herewith not already accounted for, please charge such fee to Deposit Account No. 19-3880 of the undersigned. Furthermore, if any extension of time not already accounted for is required, such extension is hereby petitioned for, and it is requested that any fee due for said extension be charged to the above-stated Deposit Account.

Respectfully submitted,

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